REMARKS

STATUS OF THE CLAIMS

Claims 8, 9, 11-19 and 23-30 were pending in this application. Claims 24, 25, 27, and 29 have been cancelled without prejudice. Claims 8, 11, 26, 28, and 30 have been amended. Following entry of the amendments claims 8, 9, 11-19, 23, 26, 28, 29, and 30 will be pending and at issue.

SUPPORT FOR AMENDMENTS TO THE CLAIMS

Claim 8 has been amended to include the term "wherein the T-cells are cultured in the presence of whole bovine myelin proteins or synthetic human myelin proteins." A similar amendment has been made to claim 30. Support can be found throughout the specification as filed, e.g., at page 8, lines 10-11 ("Preferably, the PBMCs obtained are cultured in presence of cow myelin proteins or synthetic complete human myelin proteins as they are identified and become available.").

Claim 11 has been amended to recite "T-cells that respond to a plurality of different myelin proteins;" similarly, claim 23 has been amended to recite "wherein said attenuated T-cells are reactive to a plurality of different myelin proteins;" claim 30 has been amended in a similar manner. Support can be found throughout the specification as filed, e.g., at page 8, lines 12-13 ("This is accomplished by culturing the cells in the presence of specific myelin antigens."); at page 11, lines 5-7 ("Cycles of restimulation and expansion were repeated weekly until the response to myelin antigens detected in proliferation assays exceeded the response to control antigens by three fold.").

Claim 26 has been amended to recite an element of cancelled claim 27; claim 28 has been amended to recite an element of cancelled claim 29.

The amendments to the claims therefore add no new matter and entry is respectfully requested.

OBJECTIONS TO THE SPECIFICATION

The specification was objected to as allegedly failing to provide proper antecedent basis

for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o).

The Examiner stated that "The method of Claims 8, 26, and 28 wherein natural and/or synthetic myelin proteins are employed, has no antecedent basis in the specification … The generic T cells cultured with generic natural or synthetic myelin proteins are not disclosed."

Regarding support for "generic natural or synthetic myelin proteins," without agreeing with the Examiner's position but rather to further prosecution, Applicant has amended the claims to recite "whole bovine myelin proteins or synthetic human myelin proteins."

Applicant disagrees that the specification does provide antecedent basis nor disclose "generic T-cells." The specification repeatedly recites "T-cells" without limiting usage of that term to T-cells from a specific source, e.g., derived from PBMCs as described in the examples and as a preferred embodiment. Support can be found at, e.g., page 6, line 20 ("Another aspect of the invention is a method of treating patients with MS by vaccinating patients with attenuated T-cells."); page 7, line 19 ("As stated above, the present invention relates to a vaccine for the treatment of MS, methods of producing the vaccine, and methods for its use. The vaccine is comprised of attenuated T-cells ..."); page 8, line 6 ("Preferably, T-cells are removed from the patient by leukapheresis."); and the claims as originally filed ("Claim 8. A method of mediating an immune response, comprising the step of administering attenuated T-cells to a human. Claim 9. The method of claim 8, wherein the T-cells are derived from autologous peripheral mononuclear cells.") Applicant should not be limited to the source of T-cells disclosed in the examples or described as a preferred embodiment.

REJECTIONS UNDER 35 U.S.C. § 112, FIRST PARAGRAPH

Claims 24, 25, and 30 stand rejected under 35 U.S.C. § 112, first paragraph, as the specification allegedly does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

Without agreeing with the Examiner's position, but rather to further prosecution,

Applicant has cancelled claims 24 and 25, rendering moot the rejection of these claims.

Applicant has both amended claim 30 and points to the specification beginning at page 10, line 13, as providing written description support for claim 30 as follows:

Claim element	Support (at page 10, lines 13-)
a) obtaining a polyclonal mixture of T-cells;	Peripheral blood mononuclear cells (PBMCs) were obtained by leukapheresis. Approximately 10^5 - 10^6 myelin protein specific T-cells can be obtained per apheresis.
b) culturing said polyclonal mixture of T-cells;	To establish autoreactive T-cell lines PBMCs were cultured in serum-free media supplemented with gentamicin …
c) stimulating said polyclonal mixture of T-cells in the presence of whole bovine myelin protein or human synthetic myelin proteins;	… and stimulated with bovine total myelin proteins prepared according to standard protocols … (see also page 8, lines 10-11 ("Preferably, the PBMCs obtained are cultured in presence of cow myelin proteins or synthetic complete human myelin proteins as they are identified and become available."))
d) expanding said polyclonal mixture of T-cells;	After 5-7 days cells were expanded using 50 U/ml of recombinant human IL-2 (Cetus). T-cell lines were re-stimulated after 10-14 days using autologous irradiated PBMCs as antigen presenting cells (APCs) and bovine myelin proteins.
e) repeating steps c and d until selecting a polyclonal subset of T cells wherein said polyclonal subset of T cells are reactive to at least two different myelin proteins; and	Cycles of restimulation and expansion were repeated weekly until the response to myelin antigens detected in proliferation assays exceeded the response to control antigens by three fold.
f) combining said polyclonal subset of T-cells with a buffer, thereby producing the attenuated T-cells for mediating an immune response in a human.	activated myelin specific T-cells were separated from APCs using Ficoll gradient separation, washed in sterile phosphate buffered saline (PBS) … Aliquots of living cells were frozen (prior to irradiation) for future injections administered every 6-12 weeks.

Clearly the specification contains sufficient written description and reasonably conveys to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the

time the application was filed. Withdrawal of this rejection is respectfully requested.

REJECTIONS UNDER 35 U.S.C. § 102

Claims 8, 9, 11, 12, 14 and 15 stand rejected under 35 U.S.C. 102(b) as allegedly anticipated by Stinissen et al. (1996). The Examiner stated that "Applicant is advised that the claims do not … recite a method employing multiple myelin proteins and, in particular, they did not, and still do not, recite a method employing multiple different myelin proteins. Accordingly, the reference which teaches the use of myelin, which is natural or synthetic, (of which more than 1 molecule was employed in the method of the reference), meets the limitations of the claims."

Applicant notes that one of skill in the art would construe the claims in view of the specification. The specification clearly differentiates Applicant's invention from the experiments described in Stinissen et al (1996) as the Stinissen experiments are described in the specification at page 6, lines 2-10 ("It also has been shown that it is possible to target and deplete a population of autoreactive T-cells involved in the autoimmune process using T-cell vaccination. Results, however, were not definitive (… and Zhang J, R Medaer, et al. (1993) Science 261:1451-1454). However, these experimental treatments for MS have targeted only myelin basic protein activated T-cells. It is highly probable that MBP-reactive T-cells represent only a small group of the autoreactive T-cells responsible for the progression of the disease."),

Accordingly, one of skill would understand that Applicant's original language "natural or synthetic myelin proteins," e.g., a plural term, is interpreted to mean that the claimed method employs multiple different myelin proteins and not a single myelin protein, e.g., MBP, as taught by Stinissen (e.g., Zhang).

However, in order to further prosecution, Applicant has amended claim 8 to recite "wherein the T cells are cultured in the presence of whole bovine myelin proteins or synthetic human myelin proteins." Claims 9, 11, 12, 14 and 15 depend on claim 8. Stinissen clearly does not include this element and therefore cannot anticipate the claims. Applicant respectfully requests withdrawal of this rejection.

REJECTIONS UNDER 35 U.S.C. § 103

Claims 16-19 were rejected under 35 U.S.C. 103(a) each as allegedly unpatentable over Stinissen et al. (1996). Applicant respectfully disagrees for the reasons discussed above regarding Stinissen, as claims 16-19 depend on claim 8. Applicant respectfully requests withdrawal of this rejection.

Claim 13 was rejected under 35 U.S.C. 103(a) each as allegedly unpatentable over Stinissen et al. (1996) in view of Correale et al (1995). Applicant respectfully disagrees for the reasons discussed above regarding Stinissen, as claim 13 depends on claim 8. Correale does not remedy the defects of Stinissen, and the combination of art does not include all elements of the claims. Applicant respectfully requests withdrawal of this rejection.

CONCLUSION

Withdrawal of the pending rejections and reconsideration of the claims are respectfully requested, and a notice of allowance is earnestly solicited. If the Examiner has any questions concerning this Response, the Examiner is invited to telephone Applicant's representative at (415) 875-2316.

Respectfully submitted,
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